Candidiasis (Invasive)

Candidiasis is infection by *Candida* species (most often *C. albicans*), manifested by mucocutaneous lesions, fungemia, and sometimes focal infection of multiple sites. Symptoms depend on the site of infection and include dysphagia, skin and mucosal lesions, blindness, vaginal symptoms (itching, burning, discharge), fever, shock, oliguria, renal shutdown, and disseminated intravascular coagulation. Diagnosis is confirmed by histopathology and cultures from normally sterile sites. Treatment is with amphotericin B, fluconazole, echinocandins, voriconazole, or posaconazole.

Candida species are commensal organisms that inhabit the gastrointestinal (GI) tract and sometimes the skin (see etiology of mucocutaneous candidiasis). Unlike other systemic mycoses, candidiasis results from endogenous organisms. Most infections are caused by *C. albicans*; however, *C. glabrata* (formerly *Torulopsis glabrata*) and other non-albicans species are increasingly involved in fungemia, urinary tract infections, and, occasionally, other focal disease. *C. glabrata* is frequently less susceptible to fluconazole than other species; *C. krusei* is inherently resistant to fluconazole; frequency of resistance to voriconazole and amphotericin varies. *C. krusei* is most frequently susceptible to echinocandins. *C. auris* is an emerging, multidrug-resistant species that has caused recent outbreaks in hospitals and is challenging to identify and treat.

Candida species account for about 80% of major systemic fungal infections and are the most common cause of fungal infections in immunocompromised patients. Candidal infections are one of the most common hospital-acquired infections. Because resistance and transmission of *C. auris* in health care facilities have

become a concern, special infection control precautions have been instituted for patients who are colonized or infected with *C. auris*.

Candidiasis of the esophagus is a defining opportunistic infection in AIDS. Although mucocutaneous candidiasis is frequently present in HIV-infected patients, hematogenous dissemination is unusual unless other specific risk factors are present

Disseminated candidiasis

Neutropenic patients (eg, those receiving cancer chemotherapy) are at high risk of developing life-threatening disseminated candidiasis.

Candidemia may occur in nonneutropenic patients during prolonged hospitalization. This bloodstream infection is often related to one or more of the following:

- Central venous catheters
- Major surgery
- Broad-spectrum antibacterial therapy
- IV hyperalimentation

IV lines and the GI tract are the usual portals of entry.

Candidemia often prolongs hospitalization and increases mortality due to concurrent disorders. Candidemia may occur with other forms of invasive candidiasis, such as endocarditis or meningitis, as well as focal involvement of skin, subcutaneous tissues, bones, joints, liver, spleen, kidneys, eyes, and other tissues. Endocarditis is commonly related to IV drug abuse, valve replacement, or intravascular trauma induced by indwelling IV catheters.

All forms of disseminated candidiasis should be considered serious, progressive, and potentially fatal.

Symptoms and Signs

Esophageal candidiasis is most often manifested by dysphagia.

Candidemia usually causes fever, but no symptoms are specific. Some patients develop a syndrome resembling bacterial sepsis, with a fulminating course that may include shock, oliguria, renal shutdown, and disseminated intravascular coagulation.

Candidal endophthalmitis starts as white retinal lesions that are initially asymptomatic but can progress, opacifying the vitreous and causing potentially irreversible scarring and blindness. In neutropenic patients, retinal hemorrhages occasionally also occur, but actual infection of the eye is rare.

Papulonodular skin lesions may also develop, especially in neutropenic patients, in whom they indicate widespread hematogenous dissemination to other organs. Symptoms of other focal or invasive infection depend on the organ involved.

Diagnosis

- Histopathology and fungal cultures
- Blood cultures
- Serum beta-glucan testing
- T2Candida panel

Because *Candida* species are commensal, their culture from sputum, the mouth, the vagina, urine, stool, or skin does not necessarily signify an invasive,

progressive infection. A characteristic clinical lesion must also be present, histopathologic evidence of tissue invasion (eg, yeasts, pseudohyphae, or hyphae in tissue specimens) must be documented, and other etiologies must be excluded. Positive cultures of specimens taken from normally sterile sites, such as blood, cerebrospinal fluid, pericardium, pericardial fluid, or biopsied tissue, provide definitive evidence that systemic therapy is needed.

Serum beta-glucan is often positive in patients with invasive candidiasis; conversely, a negative result indicates low likelihood of systemic infection.

The T2Candida panel is a magnetic resonance assay that directly detects *Candida* species in whole blood samples in 3 to 5 hours. It is highly sensitive and has an excellent negative predictive value (1). Other molecular diagnostic testing is also available, including matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry and polymerase chain reaction (PCR)-based assays.

Ophthalmologic examination to check for endophthalmitis is recommended for all patients with candidemia.

tandard laboratory techniques often misidentify *C. auris* as *C. haemulonii*, *C. famata*, *C. sake*, or another species. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) is a more reliable method for correct identification. A nucleic acid-based test also is now available.

Treatment

- An echinocandin if patients are severely or critically ill or if infection with *C. glabrata*, *C. auris*, or *C. krusei* is suspected
- Fluconazole if patients are clinically stable or if infection with *C. albicans* or *C. parapsilosis* is suspected
- Alternatively, voriconazole or amphotericin B

Invasive candidiasis

In patients with invasive candidiasis, predisposing conditions (eg, neutropenia, immunosuppression, use of broad-spectrum antibacterial antibiotics, hyperalimentation, presence of indwelling lines) should be reversed or controlled if possible.

In nonneutropenic patients, IV catheters should be removed.

When an echinocandin is indicated (if patients are moderately severely ill or critically ill [most neutropenic patients] or if *C. glabrata*, *C. auris*, or *C. krusei* is suspected), one of the following drugs can be used:

- Caspofungin, loading dose 70 mg IV, then 50 mg IV once a day
- Micafungin 100 mg IV once a day
- Anidulafungin, loading dose 200 mg IV, then 100 mg IV once a day
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If fluconazole is indicated (if patients are clinically stable or if *C. albicans* or *C. parapsilosis* is suspected), loading dose is 800 mg (12 mg/kg) orally or IV once, followed by 400 mg (6 mg/kg) once a day.

If there is intolerance, limited availability, or resistance to other antifungal drugs, a lipid formulation of amphotericin B at a dosage of 3 to 5 mg/kg IV once a day can be used .

Treatment of invasive candidiasis is continued for 14 days after the last negative blood culture.

Esophageal candidiasis

Esophageal candidiasis is treated with one of the following:

- Fluconazole 200 to 400 mg orally or IV once a day
- Itraconazole 200 mg orally once a day

If these drugs are ineffective or if infection is severe, one of the following may be used:

- Voriconazole 4 mg/kg orally or IV 2 times a day
- Posaconazole 400 mg orally 2 times a day
- An echinocandin

Treatment of esophageal candidiasis is continued for 14 to 21 days.

Key Points

- **Unlike other fungal infections, invasive candidiasis is usually due to endogenous organisms.**
- **Invasive infection typically occurs in immunocompromised and/or hospitalized patients, particularly those who have had surgery or been given broad-spectrum antibiotics.**
- **Positive cultures of specimens taken from normally sterile sites (eg, blood, cerebrospinal fluid, tissue biopsy specimens) are needed to**

distinguish invasive infection from normal colonization; serum beta-glucan is often positive in patients with invasive candidiasis.

- **A T2Candida panel on whole blood can be used to diagnose a *Candida* blood infection.**
- **Use an echinocandin if patients are severely or critically ill or if infection with *C. glabrata*, *C. auris*, or *C. krusei* is suspected.**
- **Use fluconazole if patients are clinically stable or if infection with *C. albicans* or *C. parapsilosis* is suspected.**